Remarks

I. Status of the Application and Claims

As originally filed, the present application had a total of 18 claims. These claims were rejected in a final Office Action dated July 1, 2003. In order to file an Information Disclosure Statement citing additional references, Applicants have now filed a Request for Continued Examination and are submitting the present response to the July 1 Office Action. Claims 1-18 have now been cancelled and replaced with new claims 19-29.

II. The Amendments

Support for new claim 19 may be found primarily in original claim 1. Support for the sequence identification numbers may be found on page 5 of the application, lines 7-15. Support for the treatment of pain associated with arthritis or an inflammatory condition may be found on page 2 of the application, line 29 – page 3, line 1.

Claims 20-26 all recite elements in claim 19, and are therefore supported by that claim.

Claims 27 and 28 are supported by original claim 17 and new claim 29 is supported by original claim 18.

None of the amendments made herein add new matter to the application, and their entry is therefore respectfully requested.

The Rejections

On pages 2 and 3 of the Office Action, the Examiner maintains a rejection of claims under 35 U.S.C. § 112, first paragraph. In considering Applicants' previous arguments, the Examiner argues that, even though there are two different forms of DPP IV, a 105 kDa form and a 175 kDa form, the claims are not limited to any specific form of the enzyme. In addition, the Examiner asserts that the specification does not identify the two forms of DPP IV or distinguish them from each other. Another argument made by the Examiner is that

the term "treatment" refers to correcting the causes of a disease and that Applicants' previous assertion that peptidases may be used to treat pain associated with arthritis are inappropriate, since pain is only a symptom, not the cause, of arthritis. Finally, the Examiner asserts that the application does not provide sufficient support for treating the range of conditions encompassed by the claims.

Applicants respectfully traverse this rejection for the claims as amended herein. Each of the Examiner's arguments are addressed in order below.

With respect to the allegation that the claims encompass all forms of DPP IV, Applicants have now amended claims so that they recite peptidases having specific amino acid sequences. Thus, the peptidases are unambiguously distinguished from all similar peptidases that may exist in the art. In Applicants' response of April 11, 2003, they point out that there are two different forms of DPP IV as described by Misumi, *et al.* (*Biochim. Biophys. Acta 15*:1131 (1992)) which was cited in the specification of the present application (see page 5 of the specification, lines 7-9). As discussed, this reference supports Applicants' assertion that they are referring to the membrane bound form of DPP IV which has the sequence presented as SEQ ID NO:1.[1] The teachings of the Misumi reference were incorporated into the application by reference (see page 8 of the specification). The arguments presented in Applicants' previous response are therefore relevant, and it is respectfully requested that they be considered in light of the present amendments.

With respect to the Examiner's second argument, Applicants agree that, in some contexts, it is legitimate to draw a distinction between treating the symptoms of a disease or condition and treating the disease or condition itself. However, it is also very common in other contexts to refer to a drug that alleviates one or more symptoms associated with a disease or condition simply as a treatment for the disease or condition. For example, one might refer to L-DOPA as a treatment for Parkinson's disease even though this drug does not correct the underlying cause of the disease and relief will only be temporary. Most

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[1] The reference by Misumi has already been submitted for consideration by the Examiner as Reference AM4 in the Information Disclosure Statement filed by Applicants on October 22, 2001.

importantly, the present application does not distinguish between treating pain associated with arthritis and treating the underlying mechanism causing the disease. This can be seen from the definition that is provided for the term "therapeutically effective amount" appearing on page 2 of the application, line 29 – page 3, line 1. This reads as follows:

> The term "therapeutically effective amount" is a dosage sufficient to produce a significant reduction in one or more symptoms associated with the disease of disorder being treated. For example, in the treatment of conditions such as migraine headache, neuropathic pain, arthritis and inflammatory conditions, a therapeutically effective amount would be a dosage sufficient to reduce the amount of pain or discomfort experienced by the patient.

In order to avoid any ambiguity that might exist, Applicants have now amended their claims so that they refer specifically to the treatment of pain, including arthritic pain.

Finally, the Examiner argues that the range of conditions that Applicants assert are treatable using the recited peptidases is too broad. In response, Applicants have narrowed claims so that they are now all specifically directed to the treatment of neuropathic pain, postherpetic pain, arthritic pain and pain associated with inflammatory conditions. Applicants respectfully submit that it is well established in the art that the production of substance P is associated with the transmission of pain and references are cited in the application to support this contention (see references cited on page 1, lines 15-23).[2] Since it is clear, and apparently undisputed, that DPP IV and the other peptidases are effective at degrading substance P, Applicants submit that it is entirely reasonable to conclude that these peptidases should interfere with pain signal transmission promoted by substance P. The present application cites experiments demonstrating the effectiveness of DPP IV in treating other substance P-related conditions (histamine evoked bronchoconstriction, and vasodilation induced either by histamine or directly by substance P) and the Examiner has not cited any art or provided any argument as to why extending these results to other substance P-related conditions is not warranted.

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[2] All of the references recited have been submitted to the Examiner for consideration as part of the Information Disclosure Statement filed by Applicants. Specifically, the references are cited as Documents AL2, AL3, AP3, AQ4, AL5, AN5, and AN6.

Conclusion

In light of the amendments and discussion above, Applicants submit that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims presently pending in the application be allowed.

If, in the opinion of the Examiner, a phone call may help to expedite the prosecution of this application, the Examiner is invited to call Applicants' undersigned attorney at (202) 419-7013.

Respectfully submitted,

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